UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF INDIANA
INDIANAPOLIS DIVISION

PDL BioPharma, Inc.,

Plaintiff,

v.

Eli Lilly and Company,

Defendant.

Civil Action No. _____

COMPLAINT
DEMAND FOR JURY TRIAL

COMPLAINT FOR ANTICIPATORY BREACH OF CONTRACT AND DECLARATORY JUDGMENT

Plaintiff PDL BioPharma, Inc. ("PDL") hereby alleges, for its Complaint against Defendant Eli Lilly and Company ("Lilly"), on personal knowledge as to its own actions and on information and belief as to the actions of others, as follows:

1. PDL pioneered the field of antibody humanization, the process by which an animal antibody created in the laboratory can be modified through genetic engineering techniques to avoid rejection as a foreign substance by the human immune system. This groundbreaking technology widely enabled the discovery of a new generation of targeted antibody treatments for cancer and other serious diseases. PDL broadly licensed its patent rights, know-how, and other technical information to Lilly, among many other pharmaceutical and biotechnology companies. In exchange, PDL bargained to receive royalties from Lilly on any "Licensed Product" that incorporates "PDL Technical Information" (as those terms are defined in the parties' license agreement).

2. Around 2010, Lilly humanized a mouse antibody to create donanemab, a treatment for Alzheimer's disease, using PDL's humanization technology. Lilly expects to receive FDA

approval for donanemab in early 2024. Although donanemab is a "Licensed Product" that incorporates "PDL Technical Information" under the parties' license agreement, Lilly has unequivocally repudiated its obligation to pay royalties to PDL on sales of donanemab once it receives FDA approval. In doing so, Lilly has anticipatorily breached the parties' license agreement, thereby entitling PDL to a declaratory judgment that Lilly owes royalties to PDL on sales of donanemab under the plain terms of their agreement.

The Parties

3. PDL is a corporation organized and existing under the laws of the State of Delaware, having its principal place of business at 10585 Double R Boulevard, Suite 100, Reno, Nevada, 89521. PDL dissolved on January 4, 2021, and PDL's corporate existence is currently set to expire on October 4, 2024. PDL will move to extend its corporate existence as necessary, including to pursue the claims asserted in this litigation. Under Delaware law, a dissolved corporation is "continued" for at least three years from dissolution or "for such longer period as the Court of Chancery" directs "for the purpose of prosecuting and defending suits . . . and of enabling [the corporation] gradually to settle and close their business." *See* 8 Del. Code § 278. A dissolved corporation shall "be continued as a body corporate beyond the 3-year period and until any judgments, orders or decrees therein shall be fully executed, without the necessity for any special direction to that effect by the Court of Chancery." *See id.*

4. PDL is informed and believes, and on this basis alleges, that Lilly is a Domestic For-Profit Corporation organized and existing under the laws of the State of Indiana, having its principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285.

Jurisdiction and Venue

5. PDL is informed and believes, and on that basis alleges, that this Court has personal jurisdiction over Lilly because Lilly has availed itself of the legal protections of the State of Indiana

by, among other things, incorporating in and maintaining its principal place of business in Indiana. This Court also has personal jurisdiction over Lilly because Lilly has availed itself of the legal protections of the State of Indiana by, among other things, asserting claims and admitting jurisdiction in lawsuits filed in the United States District Court for the Southern District of Indiana. *See, e.g.*, *Apotex Inc. v. Eli Lilly & Company*, No. 1:22-cv-2342, Answer (Dkt. 15) ¶¶ 4, 10-12 (S.D. Ind. Jan. 13, 2023); *Eli Lilly & Company v. Shilpa Medicare Ltd.*, No. 1:20-cv-3132, Complaint (Dkt. 1) ¶ 2 (S.D. Ind. Dec. 4, 2020); *Eli Lilly & Company v. Sensorrx*, No. 1:19-cv-4550, Complaint (Dkt. 1) ¶ 4 (S.D. Ind. Nov. 11, 2019); *Eli Lilly & Company v. Dr. Reddy's Laboratories, Ltd.*, No. 1:19-cv-1246, Complaint (Dkt. 1) ¶ 4 (S.D. Ind. Mar. 27, 2019).

6. PDL is a corporation and a citizen of the states of Delaware and Nevada. PDL is informed, and believes, and on this basis alleges, that Lilly is a Domestic For-Profit corporation and a citizen of the State of Indiana. Accordingly, this Court has diversity jurisdiction under 28 U.S.C. § 1332(a)(1) because there is complete diversity of citizenship and the amount in controversy exceeds the sum or value of $75,000, exclusive of interest and costs.

7. Venue is proper in this District pursuant to 28 U.S.C. §§ 1391(b) and (c) because Lilly resides in this District and because Lilly is subject to personal jurisdiction in this District.

Background Facts

Technical Background on Antibodies

8. Antibodies are naturally produced by cells of the immune system and represent an important component of the immune system in its fight against foreign microbes and pathogens. Antibodies bind to parts of biological compounds called antigens.

9. Antibodies are Y-shaped proteins composed of four chains of linked amino acids (which are the building blocks of all proteins). An antibody consists of two identical heavy chains and two identical light chains, named based on their relative length and weight to one another—

i.e., the heavy chain is longer (and has a higher molecular weight) than the light chain. Figure 1 below shows an antibody with two identical heavy chains (blue) and two identical light chains (orange):

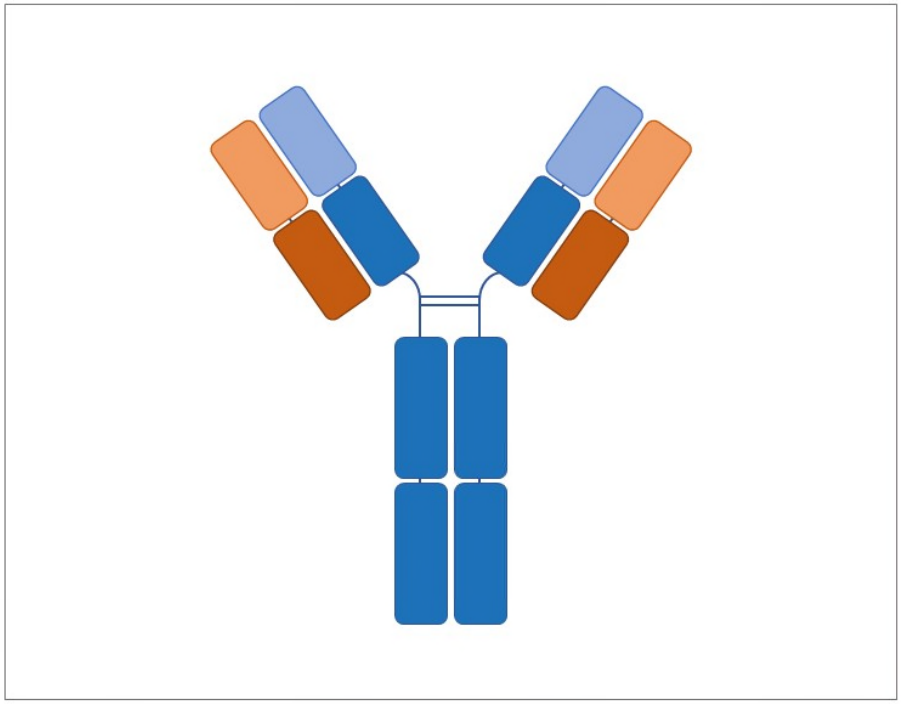

Figure 1.

10. Each chain is structurally divided into two regions with distinct functions: (1) a variable region and (2) a constant region. The variable region varies significantly between different antibodies and enables an antibody to recognize and bind to a particular antigen. The constant region is similar between different antibodies and functions to activate other immune system components. Together, the heavy and light chain variable regions allow an antibody to bind to a specific antigen, and the heavy and light chain constant regions signal the immune system to destroy that antigen. Figure 2 on the next page shows the light chain variable region (light orange),

heavy chain variable region (light blue), light chain constant region (dark orange), and heavy chain constant region (dark blue):

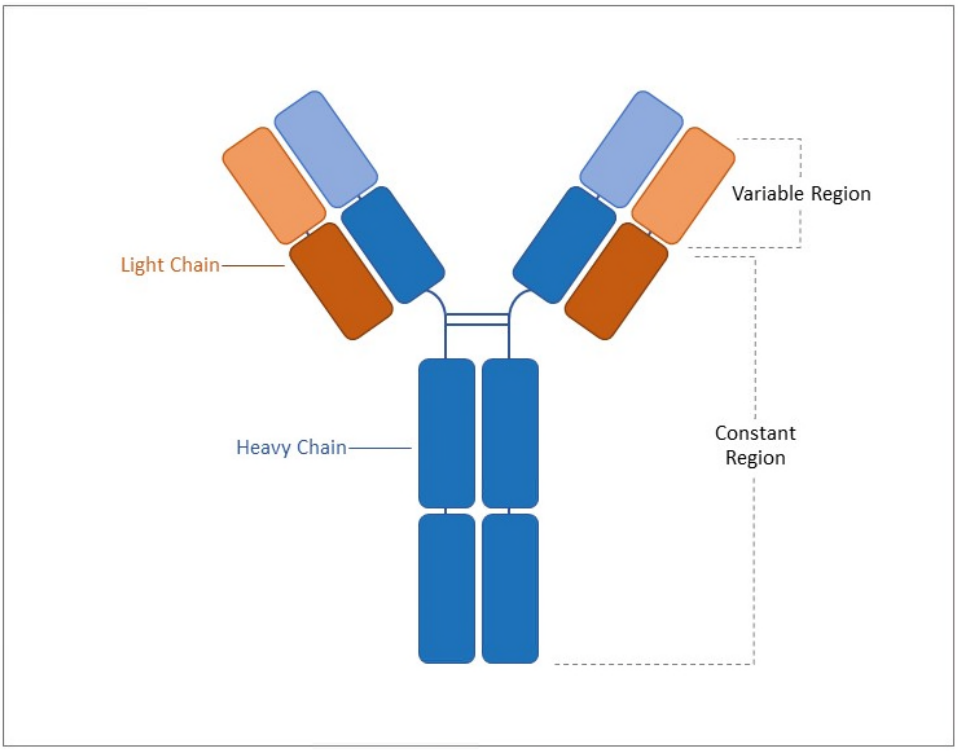

Figure 2.

11. Within each variable region of an antibody, there are complementarity determining regions ("CDRs") and framework regions ("FRs"). There are three CDRs in each variable region, which contain the most highly variable portion of the antibody. The CDRs have a particularly high degree of variability in both their amino acid sequence and in their three-dimensional structure. The CDRs are responsible for binding a specific site on an antigen. The FRs are the remaining parts of the variable region and are responsible for positioning and aligning the CDRs with the

specific site on the antigen so that the antibody and antigen can bind together. Figure 3 below provides a diagram of how the CDRs and FRs are organized:

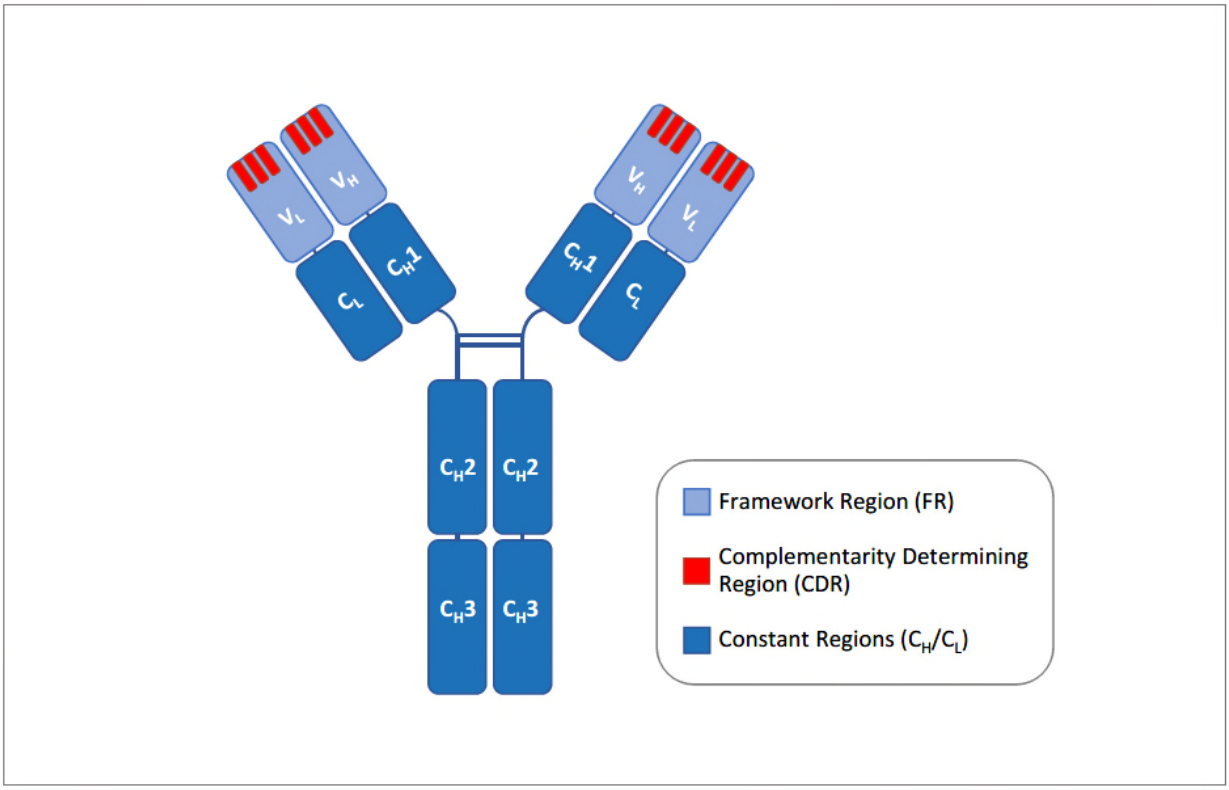

Figure 3.

Development of "Chimeric" Antibodies

12. The advent of antibody technology in the mid-1970s for the first time gave researchers and clinicians the tools to develop essentially unlimited quantities of what are called monoclonal antibodies—a colony of nearly identical antibodies capable of binding to a predetermined antigen. Monoclonal antibodies were generally produced in mice: a mouse is immunized with a particular antigen of interest, and the mouse produces antibodies to that antigen using its immune cells. The cells responsible for producing antibodies are then removed from the mouse and fused with a type of cancer cell to create what are called hybridomas. These hybridomas each continue to produce multiple, nearly identical copies of a single antibody. Monoclonal

antibodies were thought to hold great promise in, for example, the removal of harmful cells from the body.

13. Unfortunately, the development of appropriate therapeutic products based on monoclonal antibodies was severely hampered by a number of drawbacks inherent in monoclonal antibody production. The most significant drawback was that the monoclonal antibodies were nonhuman (generally, mouse or rat). Since the antibody was originally produced in mouse cells, it contained amino acid sequences that would be recognized as foreign by a human's immune system. As a result, if injected into a human, an immune response would be elicited against the antibody itself in the human, and the immune system would attack the foreign antibodies as though they were foreign antigens (instead of using them to attack the antigen that the antibody was designed to bind). The degree to which an antibody elicited that negative reaction is called "immunogenicity."

14. Researchers tried to address the immunogenicity problem with the production of "chimeric" antibodies, in which, through application of genetic-engineering techniques, the constant regions of a human antibody were combined with variable regions of a mouse antibody (or another animal). Because the animal variable regions typically came from a monoclonal antibody—which, as discussed above, could be produced to target a specific antigen—these chimeric antibodies could be engineered to target an antigen of interest. Maintaining a human constant region lowered the immunogenicity of these antibodies because a higher percentage of the antibodies were human and, therefore, not recognized by the patient's immune system as foreign. In addition, the human constant regions could more effectively interact with the human immune system. However, a significant immunogenicity problem remained because of the animal sequences in the variable regions.

Development of "Humanized" Antibodies

15. Thereafter, researchers used recombinant DNA technology to produce "humanized" antibodies. Recombinant DNA technology refers to creating DNA molecules by laboratory methods of genetic recombination that bring together genetic material from multiple sources, thereby creating sequences that would not otherwise be found in nature. Specifically, human FRs can be combined with mouse CDRs (or another animal type) to create a recombinant humanized antibody in a process sometimes called "CDR-grafting." Like the mouse antibody, the recombinant humanized antibody can target the antigen using the CDRs isolated from the mouse. But, unlike the mouse antibody, the recombinant humanized antibody will not be recognized as foreign and thus rejected by the body due to the human FRs (and human constant region). Figure 4 below shows a humanized antibody as an example:

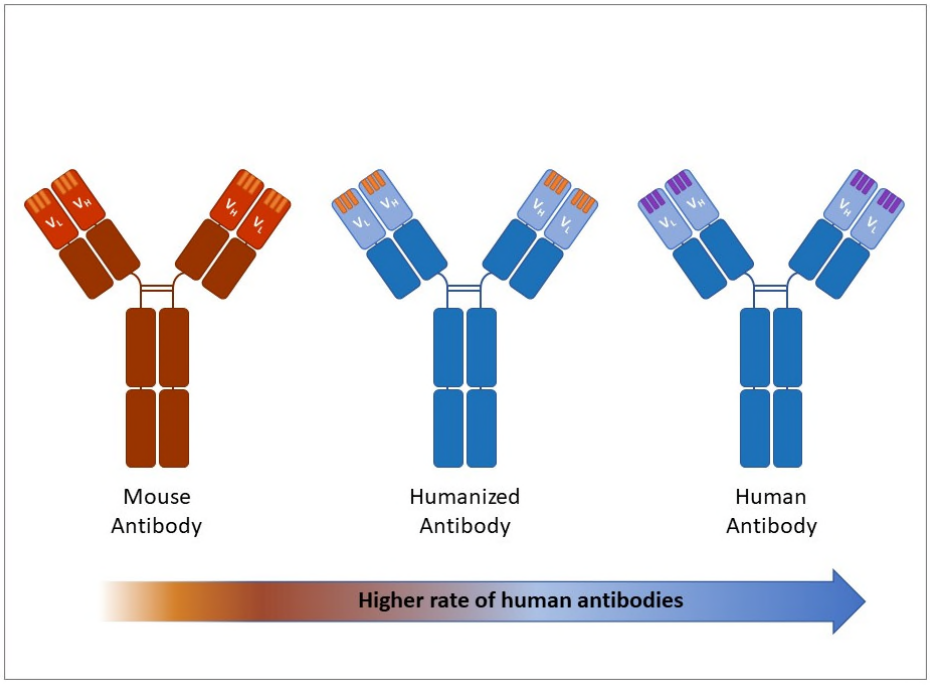

Figure 4.

16. However, a major problem with these CDR-grafting humanization procedures was loss of affinity for the antigen of interest. Affinity refers to the strength of the interaction between

the antibody and the antigen. An antibody with high affinity more avidly binds its antigen than an antibody with low affinity. Loss of any binding affinity is undesirable. At the least, it means that more of the humanized antibody will need to be injected into the patient, at higher cost and greater risk of adverse effects. Even more critically, an antibody with reduced affinity may have poorer biological functions and thus poorer therapeutic efficacy.

PDL's New Methods of Humanizing Antibodies

17. To overcome these significant problems with chimeric and existing humanized antibodies, PDL scientists developed new methods to humanize antibodies. These methods involved, among other things, substituting certain amino acids in the human FR with the corresponding mouse amino acid. PDL's humanization methods produced humanized antibodies that were substantially non-immunogenic in humans (i.e., no immune response was triggered against them) yet retained high affinity for their antigens.

18. PDL owned certain foundational patents in the United States and abroad relating to humanized antibodies and methods of making such humanized antibodies, commonly referred to as the "Queen Patents" (after Cary Queen, the lead inventor on the patents and co-founder of PDL). The Queen Patents explain how to form humanized antibodies from an animal antibody that maintains high affinity for its antigen. Due to its vast experience with humanizing antibodies, PDL also has considerable know-how and other technical information.

19. PDL broadly licensed the Queen Patents, as well as its know-how and other technical information, to many pharmaceutical and biotechnology companies, including Lilly. These companies have utilized PDL's inventions to create blockbuster drug therapies, sales of which have generated many billions of dollars in revenues, as well as substantial royalty payments to PDL.

PDL and Lilly

20. In 2000, Lilly engaged PDL to use its humanization technology and know-how to develop humanized antibodies directed against the human beta-amyloid antigen. Beta-amyloid is a protein that accumulates to form plaque found in the brain of patients with Alzheimer's Disease.

21. PDL and Lilly initially entered into a Development and License Agreement, dated September 15, 2000 (the "Agreement"), attached hereto as Exhibit 1. Pursuant to the Agreement, PDL humanized at least three anti-beta-amyloid antibodies for Lilly. PDL also provided Lilly with detailed reports, explaining how PDL scientists humanized each antibody for Lilly. For example, the humanization reports detail the design of each humanized antibody, including how human FRs were identified, the construction of each humanized antibody, including the substitutions made to the human FRs, and the binding affinity of each humanized antibody to the beta-amyloid antigen.

22. The Agreement also granted Lilly a nonexclusive, worldwide license to the Queen Patents (referred to as "PDL Patent Rights" in the Agreement) and PDL's know-how and other technical information (referred to as "PDL Technical Information" in the Agreement). Agreement at § 3.01. In exchange, Lilly agreed to make royalty payments to PDL on any Licensed Product. Agreement at § 4.02.

23. The Agreement defines "Licensed Product" as "a pharmaceutical product that incorporates substantially all of at least one (1) variable region of the Humanized Antibody(ies) developed by PDL under this Agreement." Agreement at § 1.11. The Agreement further defines "Humanized Antibody" as "the humanized form of a LILLY Antibody developed by PDL under this Agreement." *Id.* at § 1.08. In other words, a "Licensed Product" is a pharmaceutical product that incorporates substantially all of at least one variable region of an anti-beta-amyloid antibody humanized by PDL for Lilly.

24. The Agreement also defines "PDL Technical Information" as "any and all inventions, discoveries, know-how, trade secrets, information, experience, technical data, formulas, procedures, results or materials (including any biological materials and samples) which are rightfully held by PDL and which technical information is necessary for the research, development, registration, manufacture, use or sale of the Humanized Antibody." Agreement at § 1.20.

25. The parties subsequently entered into Amendment No. 1 to the Agreement, dated August 11, 2009 (the "Amendment"), attached hereto as Exhibit 2. The Amendment governs royalties and obligates Lilly to pay PDL "[a] royalty . . . of Net Sales . . . of Licensed Product sold by LILLY, . . . which incorporates the PDL Technical Information." Amendment at § 2(a)(1).

26. As explained above, PDL humanized certain antibodies for Lilly. Each of these humanized antibodies is for the treatment of Alzheimer's disease and targets the beta-amyloid antigen. One of these antibodies, also known as solanezumab, was patented by Lilly as U.S. Patent No. 7,295,761. Lilly conducted various clinical trials for solanezumab, but the Phase III studies did not meet their primary or secondary endpoints. The failure of solanezumab was not related to its humanization. Rather, according to Lilly, solanezumab failed because it only binds to soluble beta-amyloid protein and, as a result, does not remove beta-amyloid plaques. Lilly halted further clinical development of solanezumab in March 2023. PDL is informed and believes, and on that basis alleges, that the other antibodies humanized by PDL for Lilly were never patented, and clinical trials for them were never conducted.

Donanemab

27. Around 2010, while clinical trials were ongoing for solanezumab and prior to the expiration of the Queen Patents, Lilly humanized an antibody for the treatment of Alzheimer's disease, called donanemab. Like the antibodies humanized by PDL for Lilly, donanemab targets

the beta-amyloid antigen. Donanemab binds to the same site on the beta-amyloid antigen as one of these antibodies and a similar site on the beta-amyloid antigen as another of these antibodies. Unlike solanezumab, however, donanemab specifically targets and removes beta-amyloid plaques.

28. Donanemab is a "Licensed Product" under the Agreement because it is "a pharmaceutical product that incorporates substantially all of at least one (1) variable region of the Humanized Antibody(ies) developed by PDL under this Agreement"—specifically, donanemab incorporates substantially all of the variable light chain region of one or more of the antibodies humanized by PDL for Lilly.

29. PDL is informed and believes, and on that basis alleges, that donanemab also incorporates "PDL Technical Information" because it was humanized using PDL's humanization process. U.S. Patent No. 8,679,498 (the "'498 patent"), assigned to Lilly, describes donanemab and shares a common inventor (Ronald Demattos of Lilly) with the solanezumab patent. The '498 patent references PDL's humanization process, stating that "the [animal] antibody compound CDRs are grafted into a human framework that has a high sequence identity with the [animal] antibody compound framework" and that "the [human] framework can be back-mutated to the [animal] framework at certain positions based on specific criteria disclosed by Queen et al. (1991) *Proc. Natl. Acad. Sci. USA* 88:2869." '498 patent at 7:42-67. Example 1 of the '498 patent then describes the humanization process for donanemab, which is consistent with PDL's humanization process. *See id.* at 9:22-11:18.

30. According to Example 1, CDRs of mouse antibody me8 were grafted onto human FRs VH1-69/JH6 and Vk-A18/JK2 to create recombinant antibody hE8-C6. *Id.* at 9:53-56. Example 1 notes that further affinity optimization and beneficial mutations (what Queen et al. referred to as "substitutions") were performed, but without any further explanation. *Id.* at 9:56-59.

Example 1 also notes a second round of optimization using computer modeling. *Id.* at 9:60-10:43. Structural modeling discovered a steric clash between an amino acid in the light chain FR and amino acids in the heavy chain CDR, and mutation Y36L was introduced to the light chain FR. *Id.* at 10:24-27. This substitution practices one of the inventions of the Queen Patents. The resultant antibody, referred to as Antibody I (or B12L) in the '498 patent, is donanemab.

31. Because donanemab is a "Licensed Product" that incorporates "PDL Technical Information," Lilly will owe PDL a royalty pursuant to the Amendment. On March 22, 2023, PDL wrote Lilly, explaining that donanemab is a Licensed Product.

32. Lilly disagreed. The parties eventually exchanged multiple letters (in total, six letters) on the issue, but were unable to come to an agreement as to whether donanemab is a "Licensed Product" that incorporates "PDL Technical Information." As a result, Lilly has indicated that it does not intend to pay royalties to PDL for donanemab.

33. Lilly shared the results of donanemab's Phase III clinical trial at the 2023 Alzheimer's Association International Conference on July 17, 2023, and simultaneously published those results in the Journal of American Medicine Association. Lilly reported that it completed its application to the United States Food and Drug Administration ("FDA") for donanemab in Q2 2023. At its Q3 2023 Earnings Call, Lilly noted that it expected FDA approval of donanemab for the treatment of Alzheimer's disease in Q1 2024.

COUNT I

Anticipatory Breach of Contract

34. PDL realleges and incorporates the allegations in paragraphs 1 through 33 as if fully set forth herein.

35. The Agreement is governed by California law.

36. Under California law, "an anticipatory breach of contract occurs when the contract is repudiated by the promisor before the promisor's performance under the contract is due." *Central Valley General Hospital v. Smith*, 162 Cal. App. 4th 501, 514 (2008). "The repudiation may be express," and "[a]n express repudiation is a clear, positive, unequivocal refusal to perform." *Taylor v. Johnston*, 15 Cal. 3d 130, 137 (1975).

37. PDL's correspondence to Lilly explained that donanemab is a "Licensed Product" that incorporates "PDL Technical Information" under the Agreement. In response, Lilly unequivocally stated that donanemab is not a "Licensed Product" and that it does not incorporate "PDL Technical information." Lilly also unequivocally stated that it will not pay royalties to PDL on sales of donanemab. Accordingly, Lilly has expressly repudiated the Agreement and anticipatorily breached Section 4.09 of the Agreement, which requires Lilly to make its first royalty payment to PDL "within sixty (60) days after the close of each Calendar Quarter during the term of this Agreement, beginning with the Calendar Quarter in which the date of First Commercial Sale following regulatory approval occurs." Lilly has also expressly repudiated the Agreement and anticipatorily breached Section 4.10 of the Agreement, which obligates Lilly to provide notification of marketing approval "within sixty (60) days after . . . marketing approval of a Licensed Product . . . is obtained."

COUNT II

Declaratory Relief Pursuant to 28 U.S.C. § 2201(a)

38. PDL realleges and incorporates the allegations in paragraphs 1 through 37 as if fully set forth herein.

39. Donanemab is a "Licensed Product" under the Agreement because it incorporates substantially all of the variable light chain regions of one or more of the antibodies humanized by PDL for Lilly. In correspondence, Lilly has stated that donanemab is not a "Licensed Product."

PDL requests a declaratory judgment that donanemab is a "Licensed Product" under the Agreement.

40. Donanemab incorporates "PDL Technical Information" because it was humanized according to PDL's patented humanization techniques. Lilly has stated that donanemab does not incorporate "PDL Technical Information" with reference to Example 1 of the '498 patent and because PDL had no role in the humanization of donanemab. However, as discussed above, to the extent Example 1 includes the requisite level of detail to determine whether donanemab incorporates PDL Technical Information, it supports PDL's position that Lilly used "PDL Technical Information." PDL requests a declaratory judgment that donanemab incorporates "PDL Technical Information" as defined in the Agreement.

41. Lilly has indicated that it expects donanemab to be approved by the FDA in Q1 2024. As a result, Lilly's first royalty payment will be due on or around May 30, 2024. PDL requests a declaratory judgment that a royalty is owed to PDL for donanemab under the terms of the Amendment.

Prayer for Relief

WHEREFORE, PDL prays for relief as follows:

A. Judgment that Lilly anticipatorily breached the Agreement;

B. An award of damages;

C. A declaration that donanemab is a "Licensed Product" under the Agreement;

D. A declaration that donanemab incorporates "PDL Technical Information" as defined in the Agreement;

E. A declaration that royalties on donanemab are owed to PDL under the Amendment; and

F. An award of such other and further relief as the Court may deem proper.

Jury Demand

Pursuant to Rule 38 of the Federal Rules of Civil Procedure, PDL demands trial by jury of all issues so triable by a jury in this action.

Dated: December 21, 2023

WILKINSON, GOELLER, MODESITT, WILKINSON & DRUMMY, LLP

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